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THERMODYNAMICS IN ORGAN MORPHOGENESIS

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-- ABSTRACT --

現世の万物は全て仮の姿であり、その本質は同一である。

Nothing better than this abstract.

The major concern of this article is a change in thermal non-equilibrium state through instability phenomena which is observed only in biological systems. A variational system possessing the Liapunoff's functional for either conservative or non-conservative variables undergoes a phase transition whereas a system far from thermal equilibrium, not possessing the functional, undergoes a bifurcation. Not only the Cahn's equation for a conservative variable and the Ginzburg-Landau's equation for a non-conservative variable in phase transition but also the diffusion-driven equations associated with bifurcation are, in common, derived from a master equation in the stochastic theory under the isothermal and isobaric conditions. We now remark the following distinction between physical and biological systems. While no thermal state develops in any physical systems, we observe a dissipative state far from thermal equilibrium becoming a variational state in a biological system. This change in thermal non-equilibrium state may be essential in the organ development and differentiation. We now concentrate our attention on the reaction-diffusion system where the dimension, size, geometric form and boundary conditions imposed are not specified. It takes a generic form of

$$\frac{\partial \mathbf{X}}{\partial t} = F(\mathbf{X}, \mu) + \mathbf{D}\nabla^2\mathbf{X} \qquad (1)$$

where $\mathbf{X}$ and μ are respectively a n-dimensional real vector and real scalar parameter. For the linear stability analysis we express the reaction-diffusion equation (1) in terms of the space and time dependent deviation $\mathbf{u}(\mathbf{r}, t)$ from the uniform steady state solution $\mathbf{X}_o$, defined by $\mathbf{u} = \mathbf{X} - \mathbf{X}_o$;

$$\frac{\partial \mathbf{u}}{\partial t} = (L + \nabla^2)\mathbf{u} + \mathbf{Muu} + \mathbf{Nuuu} + \ldots\ldots, \qquad (2)$$

where L denotes the Jacobian matrix whose ij-th element is given by

$$L_{ij} = \frac{\partial F(\mathbf{X}_o)}{\partial X_{o_j}} \quad ;$$

the abbrevations **Muu** and **Nuuu**, etc. indicate vectors whose i-th components are given by

$$(\mathbf{Muu})_i = \frac{1}{2!}\frac{\partial^2 F_i(\mathbf{X}_\circ)}{\partial X_{\circ j}\,\partial X_{\circ k}} u_j u_k$$

$$(\mathbf{Nuuu})_i = \frac{1}{3!}\frac{\partial^3 F_i(\mathbf{X}_\circ)}{\partial X_{\circ j}\,\partial X_{\circ k}\,\partial X_{\circ l}} u_j u_k u_l \qquad (3)$$

We now obey to the mathematical procedures by Kuramoto and Tsuzuki (1974) and Kuramoto (1984). Since in the vicinity of critical point the matrix L may be developed in powers of μ, L can be written in a power-series expansion by μ. With introduction of small positive parameter defined by $\varepsilon^2\chi = \mu$, the expansion of not only L but also M and N are then of the form

$$L = L_0 + \varepsilon^2\chi\, L_1 + \ldots\ldots\ldots$$

$$M = M_0 + \varepsilon^2\chi\, M_1 + \ldots\ldots\ldots$$

$$N = N_0 + \varepsilon^2\chi\, N_1 + \ldots\ldots\ldots \qquad (4)$$

It would be appropriate to introduce a scaled time τ via $\tau = \varepsilon^2 t$ and a scaled space coordinates via $\mathbf{s} = \varepsilon\mathbf{r}$, and correspondingly, the differentiation of time and space in Eq (2) should be transformed as

$$\frac{\partial}{\partial t} \longrightarrow \frac{\partial}{\partial t'} + \varepsilon^2 \frac{\partial}{\partial \tau} \tag{5}$$

and

$$\nabla_r \longrightarrow \nabla_{r'} + \varepsilon \nabla_s \tag{6}$$

Thus we can regard **u** as dependence on the two scaled space-coordinates (**r'**, **s**) as well as the two time scales (t', τ). We may further assume the expansion of

$$\mathbf{u} = \varepsilon \mathbf{u}_1 + \varepsilon^2 \mathbf{u}_2 + \ldots\ldots. \tag{7}$$

With the substitution of (4) - (7), Eq (2) can be recast by

$$\left(\frac{\partial}{\partial t'} + \varepsilon^2 \frac{\partial}{\partial \tau} - \mathbf{D}\, \nabla^2{}_{r'} - 2\varepsilon\, \nabla_r \nabla_s - \varepsilon^2\, \mathbf{D}\, \nabla^2{}_s - L_0 - \varepsilon^2 \chi\, L_1 \right)\left(\varepsilon \mathbf{u}_1 + \varepsilon^2 \mathbf{u}_2 \right) = \varepsilon^2 M_0 \mathbf{u}_1 \mathbf{u}_1 + \varepsilon^3 \left(2M_0 \mathbf{u}_1 \mathbf{u}_2 + N_0 \mathbf{u}_1 \mathbf{u}_1 \mathbf{u}_1 \right) + O(\varepsilon^4). \tag{8}$$

In the order of ε in Eq (8) we have

$$\frac{\partial \mathbf{u}_1}{\partial t'} = L_0 \mathbf{u}_1 + \mathbf{D}\, \nabla^2 \mathbf{u}_1 \qquad (9)$$

In the Turing bifurcation the eigenvector of Eq (9) should be given in the form of U exp[$\omega t'$] with the positive eigenvalue ω. Similarly, in the order of ε^2;

$$\frac{\partial \mathbf{u}_2}{\partial t'} - \mathbf{D}\, \nabla^2 \mathbf{u}_2 - L_0 \mathbf{u}_2 = M_0 \mathbf{u}_1 \mathbf{u}_1 + 2\, \nabla_r \nabla_s \mathbf{u}_1 \qquad (10)$$

and in the order of ε^3;

$$\frac{\partial \mathbf{u}_1}{\partial \tau} - \mathbf{D}\, \nabla^2 \mathbf{u}_1 - \chi L_1 \mathbf{u}_1 = 2M_0 \mathbf{u}_2 \mathbf{u}_1 + 2\nabla_r \nabla_s \mathbf{u}_2 + N_0 \mathbf{u}_1 \mathbf{u}_1 \mathbf{u}_1 \qquad (11)$$

It should be remarked that distinctively from Eqs (9) and (10), Eq (11) is written in the newly defined space and time coordinates (**s**, τ) which are characterized by the slowness parameter ε. When $\mathbf{u}_2$ is assumed to have a damping eigenvector with time τ, then one component of the order-parameters **X**, which is denoted by X_1, can obey to the dynamic equation of the form

$$\frac{\partial X_1}{\partial \tau} = \mathbf{D}\,\nabla_s^2 X_1 + (\chi L_1 + 2M_0 V) X_1 + N_0 X_1^3 \qquad (12)$$

where $\mathbf{u}_2$ is given by a constant V. Eq (12) is referred to as the Ginzburg-Landau's equation for the order-parameter X_1 in the slowness space and time coordinates ($\mathbf{s}$, τ). Eq (12) holds in the condition that the order-parameter X_1 forms a variational system after the others X_2, X_3, ... have reached the stationary steady state of $dX_2/d\tau = 0$, $dX_3/d\tau = 0$, ... in the coordinates ($\mathbf{s}$, τ).

The order-parameters $\mathbf{X}$ in the coordinates ($\mathbf{r}$, t') first undergo the Turing bifurcation to form a dissipative structure and then one of $\mathbf{X}$ comes to be in a variational system possessing the Liapunoff's function in the slowness coordinates ($\mathbf{s}$, τ). The above phenomenon takes place independently of temperature. Thus, the decrease of temperature induces a phase transition in the newly formed variational system for the order-parameter X_1. In the biological context, it implies that in the organ development the cells are gathered and condensed to form a spatial prepattern in the dissipative system, and consequently that the organ necessarily undergoes the phase transition in the variational system. That is what is referred to as the organ differentiation. The author has proposed the idea that the intensive variable analogous to temperature is the global rate of the gene expression within the cells (Horii, 1989).

The author has proposed the Horii's differential equations for the bone development in the human jaw. It is of the form

$$\frac{\partial s}{\partial t} = \zeta \frac{\partial}{\partial x}\left(s \frac{\partial a}{\partial x} \right) + \gamma s - s^3 + \beta$$

$$\frac{\partial a}{\partial t} = D \frac{\partial^2 a}{\partial x^2} - \zeta' \frac{\partial}{\partial x}\left(a \frac{\partial s}{\partial x} \right) + a - \frac{\lambda\, as}{\phi + a} \tag{13}$$

where the order-parameters s and a represent respectively the cell densities of the tooth-forming cell and bone-forming cell and D and all the Greek letters are constants. The model equations well explain the histological aspects of the bone development and its relations with the formation of the orderly structure of the dental arch (Horii, submitted to JTB). The above theory concerning the subsequent phase transition can well explain many experimental results of the bone differentiation and remodeling mechanism (Horii, in preparation).

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